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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,807	11/30/2001	Jay Short	DVSA-1005US	6627
25225	7590	09/09/2004	EXAMINER	
MORRISON & FOERSTER LLP 3811 VALLEY CENTRE DRIVE SUITE 500 SAN DIEGO, CA 92130-2332			BORIN, MICHAEL L	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/997,807

**Applicant(s)**

SHORT ET AL.

**Examiner**

Michael Borin

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 August 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 31,34,35,114,115,132-154 and 189-201 is/are pending in the application.
- 4a) Of the above claim(s) 35,132,133 and 136-139 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 31,34,114,115,134,140-154,189-201 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Status of Claims***

1. Amendment filed 08/27/2004 is acknowledged. First occurrence of claim 152 is canceled. Claim 201 is added. Claims 31,34,35,114,115,132-154,189-201 are pending. Claims 35,132,133,136-139 remain withdrawn from consideration as drawn to non-elected species.

Claims 31,34,114,115,134,140-154,189-201 are addressed to the extent they are drawn to the elected species, peptide SEQ ID No. 2 as peptide species, and self-assembly as way of polymerizing.

### ***Sequence Listing***

2. The Sequence Listing filed 07/14/2004 is defective and must be resubmitted.

### ***Claim Rejections - 35 USC 112, second paragraph.***

3. Claims 31,34,114,115,134,140-154,189-201 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is applied for the following reasons:

B. Claim 34 remains unclear: The base claim requires that at least one monomeric peptides includes modification (such as lipid attachment) – it is not

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clear how the method of claim 34 (directed to production of peptides using polynucleotides encoding them) can produce peptides with such attachments as recited at the end of claim 31.

D. Claim 150: As was stated in the original rejection (of claims 149-152), it is not how clear how attaching of a targeting molecule can be recited as a further step if now amended claim 31 requires that such targeting molecule have already been attached to the monomeric polypeptide before the process of polymerization.

It is further unclear where and how the targeting molecule is being attached. Applicant addresses (response, p. 13, top paragraph) various alternatives - without pointing to an adequate support in specification - that bring up more issues of scope of invention and enablement.

E. Claim 193: As was stated in the original rejection, it is not clear whether the polymer comprises nanoscale delivery device or the polymer is, itself, the nanoscale delivery device.

In response, applicant does not provide clarification, but rather informs that it is just "an alternative product", and method of claim 31 "does not necessarily result in generation of a nanoscale delivery vehicle". This does not address the issue of rejection of clear whether the polymer comprises nanoscale delivery device or the polymer is, itself, the nanoscale delivery device.

***Claim Rejections - 35 USC 112, first paragraph.***

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 31,34,114,115,134,140-154,189-201 remain rejected under 35 U.S.C. 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The rejection is maintained for the reasons of record and further in view of the following. Both applicant's response and Declaration of Dr. Barton are addressed.

Applicant submits that Figure 1 demonstrates self-assembly of peptide SEQ ID No. 2. Legend to the Figure 1 (p. 5, bottom) says that it is an electronic microphotograph of a[n unidentified] protein polymer. There is no information specifying what kind of "protein polymer" is exemplified on Fig. 1 and specification is devoid of any supplemental information on the nature of protein (and whether this protein is having SEQ ID No. 2). Therefore, Examiner can not accept assertion that schematic representation on Fig. 1 reflects assembled protein SEQ ID No. 2.

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Example 19, addressed in the Declaration, is not drawn to peptide SEQ ID No. 2. The example addresses polymerization of CanA. CanA is not peptide SEQ ID No. 2 (which is abbreviated as CanA-pep); specification p. 16, top, clearly states that CanA is a nucleic acid:

CanA and CanA\_pep stand for nucleic acid SEQ ID No. 1 and its corresponding amino acid SEQ ID No. 2

In this regard, applicant's comment "CanA, of course, refers to Seq ID Nos 1&2" (response, p. 14, last paragraph) is misleading and unsubstantiated by the disclosure of invention.

In regard to Example 20, Examiner agrees that the example describes two steps of separation of E.Coli extract. However, Examiner respectfully disagrees that the purified extract consist exclusively of one protein, namely protein SEQ ID No.2. There is no disclosure that purification went as far as dividing the extract into fractions containing individual proteins (out of plethora of proteins contained in the extract). There is no mention of any particular protein (e.g., protein SEQ ID No. 2) in Example 20; rather, it addresses "protein solution" without further clarification of its content.

Further, as was discussed in the rejection, the example describes polymerization in the presence of unidentified APolymer Primers≡ prepared from a APolymer suspension≡ (see section (vi) of the example - thus, it does not seem to be an example of self-assembly. Applicant failed to address this argument.

Furthermore, as was also discussed in the rejection, there is no evidence that the resulting product is a polymer of a peptide (or of one type of peptide) - the example presents results of polymerization as grams protein/grams of E.Coli. Applicant failed to address this argument also.

In regard to Example 21, applicant asserts that the Example illustrates "method of preparing a polypeptide polymer (comprising tubules) utilizing a monomeric polypeptide of SEQ ID No. 2 together with a lipid" (see response, p. 15, last paragraph) . First, the example does not describe polypeptide polymer comprising tubules; rather it describes "lipid tubules containing drug molecules". See p. 152, line 14. Second, there is no indication that any polymerization of protein SEQ ID No. 2 is occurring: all that disclosure says is that the lipid liposomes are subjected to heating "to initiate polymerization", but whether this "initiation" results in self-assembly of protein SEQ ID No. 2 is not clear. Contrary, the final product is described as "lipid tubules containing drug molecules"; this description does not address any peptide polymers. As to Fig 3, this schematic diagram is unrelated to Example 21, as it describes a mixture of lipid, Pyrolex monomer (not clear what it is) and drug molecule, and does not represent any protein self-assembly, assemble of protein SEQ ID No. 2 in particular.

Further, applicant addresses nanotubules comprising fusion protein made of SEQ ID No. 2 and green fluorescent protein. It is not clear what fusion protein was formed by fusing open reading frames of the components, and what monomeric

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subunits were then self-assembled. Exhibit A referred to by applicant was not allocated in the response.

Finally, Examiner maintains that even if there has been demonstration of polymers obtained by self-assembly of peptide SEQ ID No. 2, there is no sufficient enablement provided for polymers formed from conjugates of said monomeric polypeptide with "attachments", such as lipids or nucleotide derivatives, or "targeting vectors"(e.g., oligosaccharides). Examiner agrees with applicant that "the level of skill of the person of ordinary skill in the art for producing polypeptide polymers was very high" Declaration, p. 2, top paragraph. The issue, however, is not producing any peptide polymers, but conditions for peptide self-assembly. Applicant did not provide sufficient evidence that the level of skill of the person of ordinary skill in the art for self-assembly of conjugates with other biomolecules was high enough to enable self-assembly of any peptide conjugate. Instead, applicant addresses references used by Examiner to demonstrate unpredictability of prior art as outdated and not casting doubt on enabling disclosure of instant application.

In view of the above, it is the Examiners position that with the insufficient guidance and working examples and in view of unpredictability and the state of art one skilled in the art could not make and/or use the invention with the claimed breadth without an undue amount of experimentation.



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5. Claim 193 (erroneously addressed in previous Office action as claims 134,135 ) remains rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claim 193 introduces new matter as it uses the phrase "polymer comprises nanoscale delivery vehicle".

Applicant argues that specification provides adequate support for the claim language. Examiner disagrees. p. 3 cited by applicant is description of Background information. Figure 2 is a diagram (not a factual representation of an obtained product) of what is presumed to be a "nanoscale delivery device"; this diagram shows "nanoscale device" comprising peptide, which is not the same as the claim language addressing, in reverse, "polymer comprising nanoscale delivery vehicle". There is no representation of a polymer which comprises nanoscale delivery vehicle in it.

***Conclusion.***

6. No claims are allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'M. Borin', with a long, sweeping horizontal line extending to the right.

Michael Borin, Ph.D.  
Primary Examiner  
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